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Lymphocytic Myocarditis Presenting as Unexplained Ventricular Arrhythmias: Diagnosis With Endomyocardial Biopsy and Response to Immunosuppression

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During a period of 18 months beginning in January 1982, a total of 65 patients were referred to the Miami Heart Institute for evaluation of either aborted out of hospital sudden death, ventricular tachycardia resistant to standard clinically directed antiarrhythmic medication programs or high grade ventricular arrhythmia (Lown class ≥ IV B) with or without syncope. After complete evaluation including cardiac catheterization in all but 1 patient, 17 patients were identified in whom no obvious cardiac disease could be found. Twelve of the 17 underwent right ventricular endomyocardial biopsy. Six of the 12 biopsies demonstrated clinically unsuspected lymphocytic myocarditis (Group A). Findings in three of the remaining six biopsies were consistent with an early cardiomyopathy and in three were completely normal (Group B). Retrospective review of the clinical, laboratory, electrophysiologic, hemodynamic and angiographic data failed to identify a marker that reliably separated Group A from Group B patients.

In addition to antiarrhythmic therapy guided by laboratory electrophysiologic study, all Group A patients were treated with prednisone and azathioprine. After 6 months of immunosuppression, all patients with myocarditis were reevaluated in the hospital without antiarrhythmic medication. Ventricular tachycardia/fibrillation could not be provoked in the laboratory during repeat electrophysiologic testing in five of the six patients. Repeat myocardial biopsy after all immunosuppressive therapy had been discontinued revealed absence of inflammation associated with varying degrees of residual interstitial fibrosis. There were no deaths.

It was concluded that a patient with an otherwise clinically silent lymphocytic myocarditis can present with potentially life-threatening ventricular arrhythmias. The diagnosis can only be made with certainty by endomyocardial biopsy. Our preliminary uncontrolled observations suggest that such patients may have a beneficial electrophysiologic and histologic response to a course of immunosuppressive therapy.

The treatment of patients with recurrent ventricular tachycardia is a common and perplexing problem. With the advent of electrophysiologic testing, a formal approach to such patients has developed that, with ambulatory electrocardiography, permits accurate characterization of the arrhythmia and its hemodynamic consequences (1–3). The efficacy of specific antiarrhythmic drug programs can often be quickly assessed in the laboratory and these data, although not perfectly predictive, seem to correlate well with the long-term course of the patients (4–6). Many well designed studies (7–12) have reported the clinical and electrophysiologic characteristics of large groups of patients with ventricular tachycardia. In almost all these studies, a small group of patients is included in whom no obvious cardiac disease can be found to explain these potentially life-threatening arrhythmias.

To gain additional understanding of this problem, we reviewed our experience with a group of consecutive patients referred for study because of significant ventricular arrhythmias. After a complete cardiac evaluation including electrophysiologic testing and cardiac catheterization, those patients with no obvious cardiac disease were further studied with serial right ventricular endomyocardial biopsies. Fifty percent of these patients undergoing biopsy had a lymphocytic myocarditis that was unsuspected and otherwise clinically silent.

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Methods

Study patients. The records of the clinical electrophysiologic laboratory of the Miami Heart Institute were reviewed for the 18 month period beginning in January 1982. The hospital records of all patients who were referred for study primarily because of 1) aborted out of hospital sudden death, 2) ventricular tachycardia resistant to standard clinically directed arrhythmia medication programs, and 3) high grade ventricular arrhythmia (Lown class ≥ IV B) with or without syncope were examined.

The results of clinical examination and noninvasive studies (chest roentgenography, rest and stress electrocardiography, 24 hour ambulatory electrocardiography and echocardiography) as well as diagnostic cardiac catheterization were reviewed. All patients in whom a definite cause of the ventricular arrhythmias could not be established were selected for further study.

During the 18 month study period, a total of 65 patients were referred for evaluation. Cardiac catheterization was performed in 64 of the patients before formal electrophysiologic study. The ventricular arrhythmias were related to coronary artery disease in 40 patients, valvular heart disease in 4, primary myocardial disease in 3 and congenital heart disease (status post-tetralogy of Fallot repair) in 1 patient. None of the 65 patients had echocardiographic or angiographic evidence of arrhythmogenic right ventricular dysplasia (13).

In 17 patients, the cause of the ventricular arrhythmias remained unclear after noninvasive evaluation and cardiac catheterization. Twelve of the 17 patients underwent right ventricular biopsy. The five patients who did not undergo biopsy were seen before we became aware of the possible association between unexplained ventricular arrhythmias and lymphocytic myocarditis.

Myocardial biopsy. During the same period, we became increasingly aware that right ventricular endomyocardial biopsy in patients with otherwise unexplained ventricular arrhythmia would occasionally reveal histologic evidence of lymphocytic myocarditis (14). By July 1982, we began to recommend that all such patients undergo biopsy. The biopsy material was obtained using the percutaneous transvenous techniques described by Mason (15). Between three and six pieces of myocardium were obtained from each patient, usually from different locations within the right ventricle in an attempt to avoid false negative biopsies and to reduce the sampling error. The specimens were fixed in 2.5% phosphate-buffered (pH 7.35) glutaraldehyde at room temperature. The fixed biopsy material was then processed in the manner described by Fenoglio (16). The slides were examined independently by two cardiac pathologists who were asked to confirm or exclude the presence of lymphocytic myocarditis but who had no knowledge of the clinical problem.

The diagnosis of lymphocytic myocarditis was made if the following histologic criteria, suggested by Margaret Billingham, MD (personal communication), were noted: 1) diffuse or focal interstitial mononuclear infiltration 2) no or minimal interstitial fibrosis, 3) absence of myofiber hypertrophy, and 4) absence of bizarre-shaped myocyte nuclei. The criteria recently suggested by Edwards et al. (14) were also met.

Electrophysiologic testing. All electrophysiologic testing was performed with the patient in the fasting nonsedated state. All antiarrhythmic medication was withdrawn at least 72 hours before the study. Multiple bipolar electrode catheters were inserted for intracardiac stimulation and recording. The data were recorded on a Hewlett-Packard 3968A eight channel tape recorder and printed on a Mingograf 82 ink jet recorder. Three orthogonal surface electrocardiographic leads were recorded simultaneously with intracardiac electrograms at a paper speed of 100 mm/s. Rectangular stimuli of 1 ms duration were delivered at twice diastolic threshold by a custom-designed computer-assisted Cordis electrophysiologic stimulator (Cordis Corporation, using software designed by Edward Smith, PhD, of Cordis Corporation).

Sinus node function and atrioventricular conduction evaluation were performed using standard electrophysiologic techniques (17,18). Ventricular stimulation with up to six programmed impulses was carried out using a standardized, progressive three part stimulation protocol (19). We have shown that in our patient group, the sensitivity, specificity and predictive accuracy of the stimulation protocol utilized are 97, 85 and 92%, respectively (19). Induction of 10 or more consecutive ventricular complexes was considered a positive response for the purposes of this study.

After the induction of reproducible ventricular tachycardia/fibrillation in the laboratory using the protocol just described, patients were given lidocaine, procainamide, propranolol and diphenylhydentoin intravenously on sequential days. After each drug infusion, the entire stimulation protocol was repeated to determine whether that drug prevented the reinduction of the tachyarrhythmia. Blood levels were monitored at the time of testing if appropriate. If all standard antiarrhythmic medication failed to prevent the reinduction of ventricular tachycardia, the procedure was terminated and the patient started on treatment with oral amiodarone. In all patients, the efficacy of the antiarrhythmic program selected was reconfirmed by multiple 24 hour electrocardiographic recordings and follow-up exercise treadmill testing.

In addition, patients whose endomyocardial biopsy revealed lymphocytic myocarditis were started on the program of immunosuppressive therapy with prednisone and azathioprine suggested by Mason and Billingham (20). Briefly, therapy was divided into three phases: initial therapy, dose tapering and maintenance treatment.

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Immunosuppressive therapy. Initially, prednisone, 1 mg/kg per day, and azathioprine, 1.25 mg/kg per day, were administered. After 1 week, the dose of prednisone was slowly decreased over 3 to 6 weeks until a maintenance dose of 0.3 mg/kg per day was reached. The dose of azathioprine was left unchanged unless the patient developed leukopenia. Maintenance therapy was then continued for at least 6 months. Repeat endomyocardial biopsy was performed during maintenance therapy to be certain that the lower doses of immunosuppression effectively eliminated the inflammation. Biopsy was repeated once again after all immunosuppressive therapy was discontinued to determine the extent of residual inflammation and fibrosis.

Follow-up. After the course of immunosuppressive therapy, all patients were readmitted for repeat electrophysiologic study. Before the study, all antiarrhythmic medication was withheld during constant electrocardiographic monitoring. The protocol and stimulation sequence of the follow-up electrophysiologic study were the same as that of the pretreatment one.

Statistical methods. Student's *t* test was used to compare the ages, duration of illness, left ventricular ejection fraction and left ventricular filling pressure of the study patients.

Results

Myocardial biopsy. Six of the 12 patients undergoing biopsy had the diagnosis of lymphocytic myocarditis confirmed histologically (Group A). The remaining six had no evidence of myocarditis (Group B). In three of these latter six patients, myocellular hypertrophy associated with interstitial and perivascular fibrosis was noted. Although these findings were not specific, they were thought to be consistent with cardiomyopathy (21). The remaining three biopsies were considered histologically normal. No patient in either group had an eosinophilic infiltrate noted on biopsy, as has been reported with drug-induced hypersensitivity myocarditis (22).

Clinical data (Table 1). No patient in either Group A or B was febrile. The duration of illness in the patients with myocarditis tended to be less than in those whose biopsies showed no evidence of inflammation (5.4 versus 26.8 months), but this difference was not statistically significant. Five of the six patients with myocarditis reported an atypical nonanginal-like chest pain. Four of the six without myocarditis reported similar pain. No aspect of the historical data reliably predicted which patients would have lymphocytic myocarditis on biopsy.

Laboratory data (Table 2). No patient in either Group A or B had an abnormally elevated erythrocyte sedimentation rate. Two patients with myocarditis (Group A) who were successfully resuscitated using direct current countershock had elevations of both serum total creatine kinase and its myocardial isoenzyme. In one of these patients, the initial white blood count was elevated but promptly returned to normal after hospitalization. The remaining four patients in Group A who did not undergo electrical defibrillation just before hospital admission had a normal white blood count, erythrocyte sedimentation rate and cardiac enzyme profile. In only two of the six patients with myocarditis was serum drawn in the acute and convalescent stages to obtain evidence of recent toxoplasmosis or viral illness; in both patients, the titers were normal. No patient in the myocarditis group (Group A) had a gallium myocardial scan performed. All six patients in the myocarditis group had normal antinuclear antibody titers. No clinical marker studied reliably predicted the presence of myocarditis histologically.

Catheterization data (Table 3). With the exception of one patient in Group B, all patients underwent complete

Table 1. Clinical Data

	Group A (6 patients with myocarditis)	Group B (6 patients without myocarditis)
Age (yr)	28 to 62 (mean 47 7)*	17 to 71 (mean 44.5)*
Male	5	3
Anginal chest pain	0	0
Atypical chest pain	5	4
Fever	0	0
Congestive heart failure	1	1
Palpitation	6	6
Syncope	2	2
Cardiac arrest	2	2
Viral illness	4	1
Duration of illness (mo)	1 to 12 (mean 5.4)*	1 to 120 (mean 26.8)*

*Probability value not significant.

Table 2. Laboratory Data

	Group A (6 patients with myocarditis)	Group B (6 patients without myocarditis)
Cardiac enlargement (CXR)	0 of 6	2 of 6
Cardiac enlargement (echo)	0 of 4	1 of 5
ST-T wave changes (ECG)	1 of 6	3 of 6
Leukocytosis	1 of 6	0 of 6
Abnormal sedimentation rate	0 of 6	0 of 5
Elevated CK	2 of 6	0 of 6
Elevated CK-MB	2 of 6	0 of 6
Abnormal gallium scan	0 of 0	0 of 2
Abnormal viral titers	0 of 2	0 of 1
Abnormal toxoplasmosis titers	0 of 2	0 of 1

CK = serum creatine kinase; CK-M = myocardial creatine kinase isoenzyme; CXR = chest X-ray film; ECG = electrocardiogram; echo = echocardiogram.

Table 3. Catheterization Data

	Group A (6 patients with myocarditis)	Group B (6 patients without myocarditis)
Catheterization performed	6 of 6	5 of 6
Normal coronary arteries	6 of 6	5 of 5
LV filling pressure (mm Hg)	10 to 20 (mean 12)*	6 to 11 (mean 9)*
Ejection fraction (%)	44 to 69 (mean 59 3)*	40 to 72 (mean 57.9)*
Normal ejection fraction (≥60%)	4 of 6	3 of 6

*p = NS; LV = left ventricular.

cardiac catheterization with coronary angiography. The one patient not catheterized was a 17 year old youth whose complete noninvasive evaluation was normal and who was presumed not to have coronary atherosclerosis. By study design all catheterized patients had normal coronary arteries. There was no significant difference between the myocarditis group (Group A) and nonmyocarditis group (Group B) in left ventricular filling pressures and global ejection fraction. Four of the six patients with myocarditis had a normal ejection fraction (≥ 60%), compared with three of the six in the nonmyocarditis group. There were no hemodynamic or angiographic markers that distinguished the myocarditis from the nonmyocarditis group.

Electrophysiologic testing (Table 4). No complications resulted from the study protocol. All patients in both Group A and B had high grade ventricular arrhythmia (Lown classification ≥ IV B). Three patients in each group had nonsustained runs of ventricular tachycardia reported on a 24 hour ambulatory electrocardiogram. Five of the six patients with biopsy-proven myocarditis (Group A) underwent formal intracardiac electrophysiologic stimulation and testing. One patient refused study. Among the five patients studied, ventricular fibrillation was induced in two, and nonsustained ventricular tachycardia was induced in two. In the remaining patient, neither ventricular fibrillation nor ventricular tachycardia could be induced in the laboratory with the protocol employed.

Table 4. Electrophysiologic Data

	Group A (6 patients with myocarditis)	Group B (6 patients without myocarditis)
Stress ECG		
PVCs	4 of 5	3 of 3
VT	0 of 5	2 of 3
24 hour ECG		
PVCs	6 of 6	6 of 6
VT	3 of 6	3 of 6
EPS performed	5 of 6	5 of 6
VT not inducible	1 of 5	3 of 5
VT inducible	2 of 5	0 of 5
VF inducible	2 of 5	2 of 5
Antiarrhythmic therapy	5 of 6	6 of 6
Standard	3 of 5	4 of 6
Amiodarone	2 of 5	2 of 6
Immunosuppressive	6 of 6	0 of 6

ECG = electrocardiogram; EPS = electrophysiologic study; PVCs = premature ventricular complexes; VF = ventricular fibrillation, VT = ventricular tachycardia.

One of the six patients without myocarditis (Group B) refused study. Ventricular tachycardia could not be initiated in three of the remaining five patients in this group; ventricular fibrillation was induced in the other two. No electrophysiologic variable studied reliably distinguished the myocarditis from the nonmyocarditis group.

Antiarrhythmic therapy. Five of the six patients with myocarditis were treated with antiarrhythmic agents; these drugs were not given to the patient in whom ventricular tachycardia or fibrillation could not be induced in the laboratory. In two of the five treated patients, standard antiarrhythmic agents (procainamide in one and propranolol and diphenylhydantoin in the other) successfully protected the patients from catheter reinduction of ventricular tachycardia or fibrillation. Two patients with myocarditis (Group A) whose arrhythmias continued to be inducible in spite of conventional antiarrhythmic medications were given oral amiodarone. The one patient in the myocarditis group who refused electrophysiologic study was started empirically on oral procainamide.

Of the six patients in the nonmyocarditis group, three were adequately protected with a standard antiarrhythmic agent (procainamide) and two were given amiodarone. The patient in this group who refused electrophysiologic study was treated empirically with procainamide.

Immunosuppressive therapy. All six of the patients with myocarditis were given prednisone and azathioprine in addition to their other medications. Patients without myocarditis did not receive immunosuppressive therapy.

All patients in the myocarditis group became clinically "cushingoid" with the doses of prednisone employed. However, only one patient needed a reduction in the dose of prednisone because of the development of diabetes mellitus requiring insulin therapy and the development of a reversible steroid-induced proximal skeletal myopathy. No patient developed leukopenia requiring a reduction in the dose of azathioprine. No patient developed opportunistic infection. All six patients in this group underwent repeat myocardial biopsy when maintenance immunosuppressive therapy was reached in 6 to 8 weeks, and all six demonstrated histologic evidence of either a marked reduction or absence of inflammation, usually associated with an increase in the amount of interstitial fibrosis (Fig. 1).

Follow-up evaluation. After 6 months of immunosuppressive therapy, the patients in the myocarditis group were reevaluated in the hospital after cessation of all antiar-

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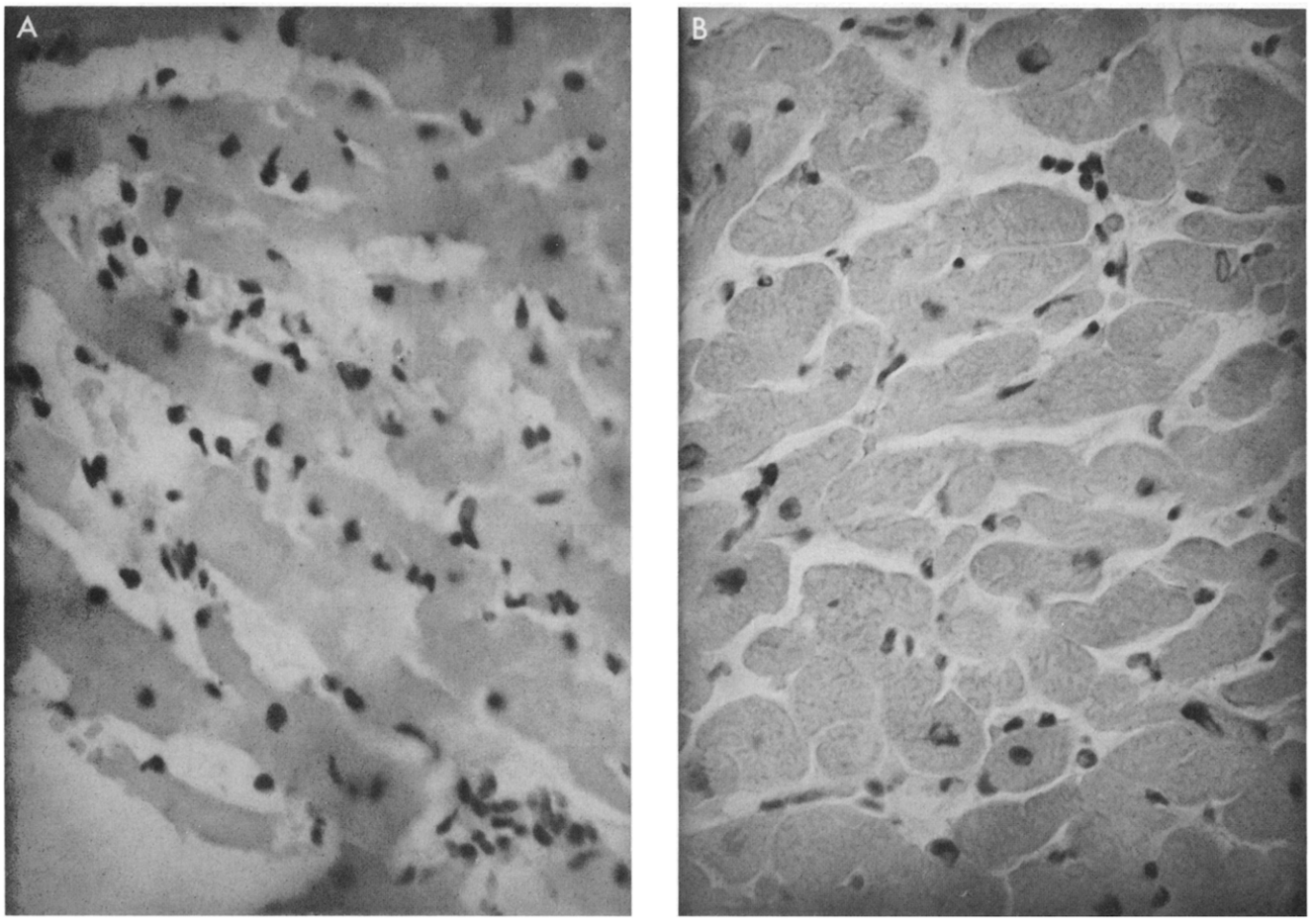

Figure 1. Right ventricular endomyocardial biopsy specimens from a patient with biopsy-proven myocarditis. **A**, Myocardial biopsy specimen before immunosuppressive therapy. A prominent mononuclear infiltrate is noted in the interstitium. **B**, Biopsy specimen after a 6 month course of prednisone and azathioprine. The interstitial infiltrate is gone. An increase in connective tissue is evident between myocytes.

rhythmic medication. Ventricular tachycardia or fibrillation could not be provoked in the laboratory during repeat electrophysiologic testing in four of the five patients (Fig. 2). Only the patient in whom the development of side effects prompted an immunosuppressive dose reduction continued to have catheter-induced ventricular tachycardia after therapy. In the remaining five patients who no longer required immunosuppression, repeat myocardial biopsy revealed absence of inflammation with varying degrees of residual interstitial fibrosis.

Discussion

Most large reported series (7–12) of patients with ventricular tachyarrhythmias contain some individuals in whom no cause for the arrhythmia can be determined despite a complete cardiac evaluation. The reported prevalence of such individuals is quite variable, ranging between 2 and 36% depending on patient selection. In the present series of 65 patients referred for evaluation of ventricular tachyarrhythmia, no definite cause could be determined in 17 of the patients (26%). Of the 12 patients who underwent myocardial biopsy, 6 had definite evidence of lymphocytic myocarditis that was otherwise clinically silent. Results of the biopsies in the remaining six patients were either completely normal or consistent with an early cardiomyopathy (21). After a course of immunosuppressive therapy, not only did the histologic evidence of myocarditis resolve, but also the ventricular tachycardia that was inducible with programmed extrastimulation could no longer be induced with the patient taking no antiarrhythmic medication.

Lymphocytic myocarditis. The clinical syndrome of acute myocarditis is well defined (23). However, the concept of a smoldering subacute or chronic myocarditis is one that is currently evolving based on the data that are now being accumulated from endoymocardial biopsy material obtained from patients with congestive heart failure of unknown cause. Mason et al. (24) reported histologic evidence of lympho-

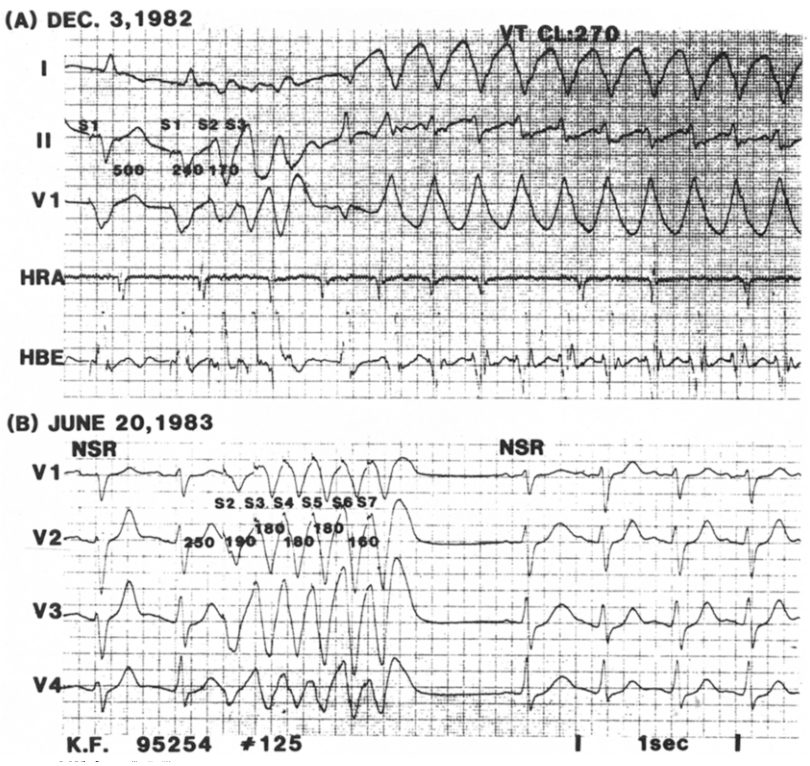

Figure 2. Electrophysiologic testing in the same patient as in Figure 1. **Panel A**, Results of testing without antiarrhythmic medication before immunosuppressive therapy. During ventricular pacing (S_1) at a cycle length (CL) of 500 ms, two programmed ventricular stimuli (S_2 and S_3) induce a monomorphic ventricular tachycardia (VT) with a cycle length of 270 ms that was similar in rate and configuration to the clinical tachycardia. **Panel B**, Repeat testing in the same patient without antiarrhythmic medication after a 6 month course of prednisone and azathioprine. The more aggressive protocol of six programmed extrastimuli (S_2,S_3,S_4,S_5, S_6,S_7) fails to initiate any repetitive response. HBE = His bundle electrogram; HRA = high right atrial electrogram; NSR = normal sinus rhythm.

cytic myocarditis in patients thought clinically to have a dilated congestive cardiomyopathy. The inflammatory process in these patients was clinically unsuspected and was only detected by endomyocardial biopsy. A small number of these patients responded to immunosuppressive therapy with hemodynamic improvement that was parallelled by histologic resolution of the infiltrate. These findings have been confirmed by others (25). More recently Fenoglio et al. (26) devised histologic classifications that seemed to predict their patients' clinical course and response to immunosuppressive therapy.

The pathogenesis of this illness is speculative. However, an increasing amount of experimental (27,28) and clinical (29,30) data would suggest that patients are infected with particular strains of myocardiotrophic viruses. After a relatively short period of time, the viruses are cleared from the myocardium. However, during the period of infectivity, the viruses alter certain myocyte proteins to produce "neo antigens" (29,31,32). In certain patients with either inherited or acquired abnormalities in suppressor T cell function, the immunologic process mediated by the cytotoxic T lymphocyte is directed against the "neo antigen" producing a continuing low grade inflammatory response that may ultimately culminate in an "idiopathic" congestive cardiomyopathy (29–35).

Unexplained ventricular arrhythmias. The concept that potentially life-threatening ventricular arrhythmias can be related to otherwise clinically silent myocarditis is intriguing. Van Hoogenhuyze et al. (36) reported on 15 patients with ventricular tachycardia in whom an underlying cardiac abnormality could not be demonstrated. Four of the 15 patients had endomyocardial biopses consistent with "chronic myocarditis." No comment was made in this preliminary report concerning treatment or follow-up. Reeder et al. (37) reported preliminary data on 17 patients with unexplained life-threatening ventricular arrhythmias, 5 of whom had myocardial biopsy findings of "myocarditis with lymphocytic infiltration and interstitial edema." Four patients received steroid therapy. Three showed resolution of the inflammation on serial biopsy. However, in two of these three patients, persistent arrhythmia required specific antiarrhythmic therapy. The results of our current study support these preliminary data. In addition, careful review of the clinical, electrocardiographic, laboratory, hemodynamic angiographic and formal electrophysiologic data of the current study suggests that the ventricular arrhythmia may be the *only* manifestation of an otherwise clinically silent myocarditis.

Recently, Strain et al. (38) reported the results of right ventricular endomyocardial biopsy in patients with spontaneous ventricular tachycardia but without apparent heart disease. Nine of their 18 patients had biopsy findings consistent with an early cardiomyopathy; 2 had diffuse abnormalities of the intramyocardial arteries, 2 had arrhythmogenic right ventricular dysplasia, 2 were normal and 3 had "subacute inflammatory myocarditis". The patients with myocarditis were not given immunosuppressive therapy and

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the investigators concluded that the "performance of right ventricular biopsies in this group of patients should be considered a research procedure." However, in our study, the histologic and clinical response of our patients to immunosuppressive therapy was both interesting and gratifying. Before immunosuppressive therapy, all had either ventricular tachycardia or had been resuscitated from cardiac arrest secondary to ventricular fibrillation. Four of the five patients studied had their clinical arrhythmia induced in the electrophysiology laboratory. After immunosuppressive therapy, clinical arrhythmias were abolished in five patients and remained unchanged in one. In four of the five patients restudied in the electrophysiology laboratory while they were not taking antiarrhythmic and antiinflammatory medication, ventricular tachyarrhythmias could not be induced using the same or a more aggressive stimulation protocol. This clinical and electrophysiologic improvement was associated with a concomitant resolution of the inflammatory infiltrate.

Cautionary points. Several cautionary points are worthy of special emphasis. The response of our patients with myocarditis to immunosuppressive therapy is uncontrolled. The natural history of this entity treated with aggressive antiarrhythmic therapy guided by electrophysiologic study without immunosuppression is unknown. It is entirely possible that both the inflammatory infiltrate and the arrhythmias would have resolved spontaneously without immunosuppression. However, it is equally possible that these patients might have eventually developed the typical picture of an "idiopathic" dilated congestive cardiomyopathy if they had not received immunosuppressive therapy. It is entirely possible that those patients who initially present with a dilated heart and congestive heart failure go through a stage in their illness before the heart dilates, in which they are at increased risk of a serious ventricular arrhythmia. The disease may be detected at this early stage only if it manifests itself by a recognized clinical arrhythmia. Finally, it should be emphasized that the natural history of our "successfully" treated patients is now unknown. They may still ultimately develop a cardiomyopathic clinical syndrome despite resolution of the infiltrate and remission of the arrhythmias. The answers to these and several other important questions require a carefully designed and controlled clinical trial with long-term clinical, electrophysiologic and histologic follow-up.

Conclusion. We have shown that clinically unsuspected myocarditis can present in the absence of cardiomegaly and congestive heart failure as otherwise unexplained, potentially life-threatening ventricular arrhythmias. None of the clinical, electrocardiographic, laboratory, hemodynamic, angiographic or electrophysiologic markers studied reliably predicted which patients had myocarditis and which did not. Because the diagnosis would have been missed if the biopsy had not been performed, we now recommend that all such patients undergo the procedure. If the biopsy reveals an active inflammatory infiltrate on the basis of the data now available, a trial of prednisone and azathioprine therapy should be started. Serial biopsies should be performed during therapy to assess its efficacy and again after therapy to assess the degree of residual fibrosis. We believe that antiarrhythmic therapy should be guided by electrophysiologic testing to be certain that adequate arrhythmia control is achieved during the course of immunosuppression. A follow-up electrophysiologic study should be performed with the patient not taking antiarrhythmic agents after immunosuppressive therapy to determine whether continued arrhythmia suppression is necessary.

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